14. Ontario Ministry of The Environment, "Scientific Criteria Document for Standard Development No. 4-84 - Polychlorinated Dibenzo-p-Dioxins and Polychlorinated Dibenzofurans," Ministry of The Environment, Toronto, March, 1986.

15. T. F. Bidleman, "Atmospheric Processes," Environ. Sci. Technol 22, 361-367 (1988).

16. T. F. Bidleman, "Gas-Particle Distribution and Atmospheric Deposition of Semi Volatile Organic Compounds," Presented at the EPA/ORNL Workshop on Risk Assessment for Municipal Waste Combustion, June 8-9, 1989.

17. T. H. Umbreit, E. J. Hesse, and M. S. Gallo, "Bioavailability of Dioxin in Soil from a 2,4,5-T Manufacturing Site," Science 232, 497-499 (1986a).

18. T. H. Umbreit, E. J. Hesse, and M. S. Gallo, "Comparative Toxicity of TCDD Contaminated Soils from Times Beach, Missouri, and Newark, New Jersey," Chemosphere 15, 2121-2124 (1986b).

19. M. Van den Berg, K. Olie, and O. Hutzinger, "Uptake and Selective Retention in Rats of Orally Administered Chlorinated Dioxins and Dibenzofurans from Fly Ash and Fly Ash Extract," Chemosphere 12, 537-544 (1983).

in the rhesus monkey study was reduced by an Uncertainty Factor of 1000 to estimate the dose limit at 1.8 pg/kg/day.

DOSE APPORTIONMENT BY MEDIUM

Since cumulative dose is relevant to dioxin effects and since there are multiple media and sources of dioxins, it was necessary to consider an apportionment approach.

Assumption. Considering the multi-media nature of dioxin exposure, the health-based limit of 1.8 pg/kg/day (based on reproductive effects as most sensitive response) should be apportioned by medium of exposure and an allowable level established for each medium. This apportionment considers potential background exposures to be significant.

Rationale. Although the background dioxin levels in the environment contribute to the total human body burden, this information was not factored in the calculation of the health-based total dose limit of 1.8 pg/kg/day. Thus the limit reflects the total theoretical permissible daily dose of dioxins from all media of exposure, including background exposure. It represents the maximum daily dose that should not be exceeded to assure that no adverse health effects occur over a lifetime of exposure to dioxins. Therefore when assessing only one of the several possible exposure media, it is necessary to apportion the health-based limit to account for other potential exposures.

The first step in apportioning multi-media exposure of humans to dioxins was to estimate the background contribution to total dioxin exposure. The average daily intake of dioxin can be estimated using a linear, one compartment model: [3]

$$\underset{(\text{ng/kg/day})}{\text{Background Dose Rate}} = \underset{(\text{ng/kg})}{\text{Body Burden}} \times \ln 2 \, / \underset{(\text{days})}{\text{half-life}}$$

Assuming that a human weighs 60 kg, has 20 percent fat, and has 7 ppt dioxin in fat (ng/kg),[12] then the body burden of dioxin is 84.0 ng. The half life is assumed to be 5.8 years (2120 days)[13] and the dose rate is estimated to be approximately 0.45 pg/kg/day. Travis and Hattemer-Frey estimated through half-life modeling and 70 kg assumption that human exposure to 2,3,7,8-TCDD is about 0.4 pg/kg/day.[3] An EPA calculation showed a range of estimates of daily intake of 2,3,7,8 - TCDD between 0.04 to 0.51 pg/kg/day. The daily dioxin intake value used by DHS is in reasonable agreement with those reported above. This background exposure at 0.45 pg/kg/day (direct and indirect) represents 25 percent of the health-based limit of 1.8 pg/kg/day.

Estimates of the relative contributions from air, food, water, and soil to the daily human exposure to dioxins were calculated from literature data. The available data on dioxin exposures were reviewed, in particular the Federal Ontario dioxin exposure assessment document.[14] This document assumed that dioxins in the Ontario environment are principally from incineration processes. Based on concentrations and contact rate the relative contributions were estimated to be: air (60%), water (5%), soil (5%), and food (30%). DHS adjusted this apportionment to account for (i) potential beef and milk exposure, and (ii) sensitive sub-groups (infants and children - milk pathway). Thus DHS estimated the relative contribution to be: air (40%), water (5%), soil (5%), and food (50%) in the Connecticut environment.

The relative source contribution of 40 percent from the air medium was

REFERENCES

1. F. C. Hart Associates, "Multiple Pathway Human Exposure and Health Risk Assessment of Polychlorinated Dibenzo-p-Dioxins and Polychlorinated Dibenzofurans from Municipal Solid Waste Incinerators," Prepared for State of Connecticut, Department of Health Services, February, 1987.

2. Connecticut Department of Environmental Protection (DEP), "Basis for Standards and Procedures and Response to Comments on Proposed Resource Recovery Regulations (Air Pollution Provisions)," (1988).

3. C. C. Travis and H. A. Hattemer-Frey, "Human Exposure to 2,3,7,8-TCDD," Chemosphere 16, 2331-2342 (1987).

4. C. C. Travis and H. A. Hattemer-Frey, "A Perspective on Dioxin Emissions from Municipal Solid Waste Incinerators," Risk Analysis 9, 91-97 (1989).

5. Environmental Protection Agency, "Health Assessment Document for Polychlorinated Dibenzo-p-dioxins," Office of Health and Environmental Assessment, May 1984.

6. F. J. Murray, F. A. Smith, K. D. Nitschke, C. G. Humiston, R. J. Kociba, and B. A. Schwetz, "Three-Generation Reproduction Study of Rats given 2,3,7,8-Tetrachlorodibenzo-p-dioxin in the Diet," Toxicology and Applied Pharmacology 50, 241-252 (1979).

7. J. R. Allen, D. A. Barsotti, L. K. Lambrecht, and J. P. Van Miller, "Reproductive Effects of Halogenated Aromatic Hydrocarbons on Nonhuman Primates," Annals of New York Academy of Sciences 320, 419-425 (1979).

8. I. C. T. Nisbet and M. B. Paxton, "Statistical Aspects of three generation studies of the reproductive toxicity of 2,3,7,8-TCDD and 2,4,5-T," The American Statistician 36, 290-298 (1982).

9. R. J. Kociba, D. G. Keyes, J. E. Beyer, R. M. Carreon, E. E. Wade, D. A. Dittenber, R. P. Kalnins, L. E. Frauson, C. N. Park, S. D. Barnard, R. A. Hummel, and C. G. Humiston, "Results of a Two-Year Chronic Toxicity and Oncogenicity Study of 2,3,7,8-TCDD," Toxicology and Applied Pharmacology 46, 279-303 (1978).

10. T. H. Umbreit, E. J. Hesse, and M. S. Gallo, "Reproductive Toxicity in Female Mice of Dioxin-Contaminated Soils from a 2,4,5 - Trichlorophenoxyacetic Acid Manufacturing Site," Archives of Environmental Contamination and Toxicology 16, 461-466 (1987).

11. J. A. Moore, M. W. Harris, and P. W. Albro, "Tissue Distribution of ^{14}C Tetrachlorodibenzo-p-dioxin in Pregnant and Neonatal Rats," Toxicology and Applied Pharmacology 37, 146-147 (1976).

12. D. G. Patterson, J. S. Holler, S. J. Smith, J. A. Liddle, E. J. Sampson and L. L. Needham, "Human Adipose Data for 2,3,7,8-TCDD in Certain U.S. Samples," Chemosphere 15, 2055-2060 (1986).

13. H. Poiger and C. Schlatter, "Pharmacokinetics of 2,3,7,8 - TCDD in Man," Chemosphere 15, 1489-1494 (1986).

Depending on the scientific assumptions used and the estimate of the carcinogenic potency of dioxin, the range of upperbounds on total risk from indirect and direct exposure to 1 pg/m^3 ranges from 2×10^{-4} ($5.5 \times 10^{-5} + 1.7 \times 10^{-4}$) to 6×10^{-6} ($1.7 \times 10^{-6} + 4 \times 10^{-6}$). In the scientific judgement of DHS, the risk was estimated to be at the lower end of the range or 6×10^{-6}. A potential risk in the 10^{-6} range is considered acceptable for an aggregate air standard for all sources of dioxin emissions. However, for individual Resource Recovery Facilities, the potential cancer risk from ambient impact is even lower and is in the 10^{-7} range. The background estimate (0.45 pg/kg/day) represents a risk in the 10^{-5} - 10^{-6} range, depending upon the assumptions used.

DISCUSSION AND CONCLUSION

Connecticut is the first state in the country to adopt a dioxin AAQS that protects the public health from the combined effects of all sources of dioxin emissions. The AAQS is an aggregate standard and is different from the "standards" of other states which are in fact only maximum allowable impacts for individual RRFs. According to Connecticut DEP, "no resource recovery facility in the state is predicted to have an ambient impact of more than 0.037 pg/m^3 dioxin equivalents." (2) This maximum predicted impact for each RRF represents about 4 percent of the AAQS, and is consistent with the limits imposed by other states (Massachusetts 0.15, Pennsylvania 0.3, Rhode Island 0.02 to 0.2, and New Hampshire 0.09 to 0.27 pg/m^3). The predicted maximum impact for each RRF in the state represents a potential upperbound carcinogenic risk in the 10^{-6} to 10^{-7} range. No adverse reproductive and immunological effects are expected to occur at this impact level. The calculated dose for 0.037 pg/m^3 impact level (direct and indirect) is 0.049 pg/kg/day and it represents about 3 percent of the health-based limit, compared with the background's 25 percent. Clearly, there is a need to identify the sources contributing to the considerable background intake, and minimize such exposure.

The non-source specific approach used in the risk assessment is a departure from incinerator-specific risk assessments. Appropriately, this approach takes into account the body burden and daily dose from all media and sources as well as the background exposures when estimating a total daily dose and comparing with the target dose limit. The target dose limit assumption facilitated apportioning the dose by media. While developing a rationale for the 40 percent air apportionment, it became apparent that the risk assessment is sensitive to the settling velocity assumption used. Inhalation (44 percent) and meat/milk ingestion (56 percent) are significant exposure pathways for a minimum particle settling velocity (0.0003 m/sec) assumption. (1) The relative significance of the inhalation exposure decreases as the settling velocity increases. At the settling velocity 0.01 m/sec, the indirect food chain pathway dominates (98 percent) although the concentration of dioxins in the air is the same. Therefore, risk assessments of this type should estimate exposures based upon several settling velocities as a means of estimating a range of potential exposures. This is particularly necessary since the location of the plant affects the settling velocity. This type of analysis will help the risk manager to assess inhalation exposure separate from indirect multiple pathway exposure, if desired. A further improvement in dioxin risk assessment would come from the knowledge of vapor/particulate phase distribution of dioxins in ambient air. This information would improve the analysis of the indirect exposure pathways, since the deposition of dioxins from the ambient air has been shown to be particle phase dominated.(16)

M115505
Enen

Risk Analysis (Accepted)
Dec. 1990

CONNECTICUT'S DIOXIN AMBIENT AIR QUALITY STANDARD

Hari V. Rao, Ph.D. and David R. Brown, Sc.D.

Connecticut Department of Health Services
Division of Environmental Epidemiology and Occupational Health
150 Washington Street
Hartford, CT

ABSTRACT

Connecticut is the first state in the country to have adopted an ambient air quality standard for dioxins at 1 pg/m^3, 2,3,7,8-TCDD equivalents, as annual average. This paper describes the scientific basis and the methodology used by the State Department of Health Services (the risk assessment agency) in assisting the Department of Environmental Protection (the risk management agency) to establish a health-based dioxin standard. This standard protects the public health from the aggregate effect of all sources of dioxin emissions in the vapor and particulate phases. The risk assessment methodology included: a limit on total daily dioxin exposure from all media and sources based on reproductive effects, a multi-media non-source specific exposure assessment, an apportionment by media of the health-based limit (including background dosing rate), an evaluation of inhalation bioavailability and cancer risk based on a calculation of a range of upperbound cancer risk estimates using different potency, bioavailability, and particle phase assumptions.

Key Words. Reproductive Effects, Multi-media Exposure, Dose Apportionment, Bioavailability, Carcinogenic Potency.

INTRODUCTION

This report describes the scientific basis for Connecticut's primary Ambient Air Quality Standard (AAQS) for dioxins established by the State Department of Environmental Protection (DEP) at 1 picogram per cubic meter (1 pg/m^3) 2,3,7,8-TCDD equivalents as annual average (a picogram is one trillionth of a gram). Dioxins and 2,3,7,8-TCDD are used interchangeably in this report. The dioxin AAQS is based on the State Department of Health Services' (DHS) analysis of a Dioxin Health Risk Assessment prepared by Hart Associates. (1) The Health Risk Assessment was prepared in response to a legislative mandate, and designed to be consistent with DEP's Air Toxics Program requirements. (2) Thus, the standard setting process was a bilateral effort, which utilized the expertise of the DHS in risk assessment, and of the DEP in risk management. A Scientific Panel served as an advisory body.

The details of the Dioxin Risk Analysis, the key assumptions used, and their rationale are presented below:

DIOXIN DAILY DOSE AND BODY BURDEN

The risk analysis developed a rationale for consideration of daily dose and body burden for dioxins which are independent of specific sources. This was considered appropriate for the following reasons:

First, dioxin exposure is multimedia in nature. Dioxins have been detected in air, soil, sediments, suspended sediments, water, fish, meat, and milk as well as in human adipose tissue, breast milk, and blood.[3,4] The total body burden represents the sum of potentially significant individual contributions from the various media, sources and routes of human exposure. By comparing the relative contributions from each medium with the health-based limit, significant exposures can be identified and necessary measures taken to reduce such exposures.

Second, the evidence suggests that there exists a background body burden of dioxins in the general population of industrialized nations.[3] The body burden measurements provide an indication of past exposure, and can be used to calculate the total daily dioxin intake from the background exposure. The health impact from this daily background exposure can be assessed, and thus incorporated into the standard setting process. However, the ways in which all of the various media, sources and routes contribute to this background exposure remain unknown. Although there are uncertainties in assessing exposures, an advantage of this approach is that it places the various media of exposure, including the overall background multi-media exposure, in perspective.

REPRODUCTIVE EFFECTS AND DOSE LIMIT

Reproductive, developmental, and carcinogenic effects were determined to be health impacts of concern and were evaluated. Animal studies on 2,3,7,8,-TCDD toxicity have clearly demonstrated that it is a developmental and reproductive toxin in a variety of species at relatively low doses. A review of the pertinent developmental and reproductive studies can be found in EPA's Health Assessment Document for PCDDs.[5] The reported adverse outcomes include reduced fertility, litter size and survival, offspring body weight changes, as well as cleft palate and kidney abnormalities. Among the available studies, Murray et al's [6] 1979 study on Sprague Dawley rats, and Allen et al's [7] 1979 study on rhesus monkeys were considered appropriate for quantitative assessment.

Murray et al's study examined the effects of dietary exposure to 2,3,7,8-TCDD on reproduction in Sprague Dawley rats over three generations. The rats were given 0, 0.001, 0.01, and 0.1 ug/kg/day. No significant toxic effects were observed in the F_0 generation during 90 days treatment prior to mating. The study showed that the lowest dose, 0.001 ug/kg/day had no effect on fertility, litter size or fetal survival. The authors concluded that the doses 0.01 and 0.1 ug/kg/day produced significant effects on the reproductive capacity through three generations, F_0, F_1, and F_2. The study indicated that the 0.001 ug/kg/day could be considered as a no effect level. A reanalysis of the Murray et al data using a different statistical approach concluded the lowest dose was an effect level and that a no effect level could not be determined. [8] Since there was a question relative to the no effect level in the rat study, DHS considered the data on 2,3,7,8-TCDD's effects on reproduction in rhesus monkeys. The doses administered in

2025546091

Ingestion Risk. The ingestion risks from the indirect exposure pathway were estimated for three deposition scenarios. The calculation assumed that 100, 80, or 40 percent of the dioxin in the ambient air is in the particle phase and that the settling velocity is 0.001 m/sec. The estimated doses, 1.0, 0.8, and 0.4 pg/kg/day were multiplied by the oral potency values to calculate the potential upperbound risks, as shown in Table 1.

Inhalation Risks. Inhalation risk assessment for the direct exposure pathway focussed on the administered dose via inhalation, 2,3,7,8,-TCDD's potency via inhalation, and the effect of the matrix factor on dioxin's potency.

Administered Dose. The concentration in the ambient air (pg/m^3) and the contact rate ($20\ m^3$/day) for a human body weight assumption (60 kg), and 100 percent pulmonary absorption determined the administered dose (pg/kg/day) via inhalation. A second calculation considered the particle/vapor nature of the airborne dioxins as well as the matrix effect and used an absorption factor of 50 percent to calculate the administered dose.

Inhalation Potency and Matrix Effect. Since 2,3,7,8-TCDD's potencies for the vapor and particulate phases via inhalation are not known, the oral potency values are used to predict the inhalation risk. This is considered a conservative approach for the following reasons:

Dioxin's potency estimates are based on the administered dose. In the lifetime feeding study the rats were given a diet mixed with dioxin dissolved in acetone matrix.[9] The bioavailability of dioxin in this matrix is reported to be 85 percent, compared with the values, 25 to 50 percent for the soil matrix,[17, 18] and 1 to 4 percent for the flyash matrix.[19] These bioavailability values are for oral/gastrointestinal absorption. The absorption values for the soil and flyash matrix indicate that considerably higher doses, 2 to 20 times higher than the dose in acetone matrix are required to produce the same dioxin concentration in the liver and elicit a tumor response. Such a shift in the dose/response curve relative to the matrix effect would predict a lower potency estimate for ingested dioxin. Thus the use of the oral potency values (acetone matrix) to predict the inhalation risk, particularly for inhaling particle bound dioxins, is considered conservative. Table 1 presents the estimated inhalation risks for 100 and 50 percent absorption assumptions.

Table 1. Dioxin Exposure and Upperbound Cancer Risk Estimates

Dose * (pg/kg/day)	Assumption	10^{-6} Risk Specific Dose (fg/kg/day) ** EPA 6	CT 36	FDA 60	EPA *** 100
Direct					
0.33	100% Abs	5.5×10^{-5}	9×10^{-6}	5.5×10^{-6}	3.3×10^{-6}
0.17	50% Abs	2.8×10^{-5}	4.5×10^{-6}	2.8×10^{-6}	1.7×10^{-6}
Indirect					
1.00	100% part	1.7×10^{-4}	2.8×10^{-5}	1.6×10^{-5}	1.0×10^{-5}
0.80	80% part	1.3×10^{-4}	2.2×10^{-5}	1.3×10^{-5}	8×10^{-6}
0.40	40% part	7×10^{-5}	1.1×10^{-5}	7×10^{-6}	4×10^{-6}

* The dose was estimated for a dioxin concentration of 1 pg/m^3, a breathing rate of 20 m^3/day and a human body weight of 60 kg.

** Femtogram (one quadrillionth of a gram).

*** Proposed potency estimate.

2025546096

derived from the worst case exposure assessment of the Ontario environment.[14] The Ontario data represent the measurements of stack air (there was no ambient air data) and the levels found in samples of fish, pork, poultry products, drinking water, human fat, and the soil in the vicinity of an incinerator. The Canadian assessment used (i) an estimated maximum annual average ambient air concentration of 8.4 pg/m^3 TCDD equivalents (60% apportioned intake); (ii) for water, a concentration of 0.002 ng/L TCDD equivalents (5% intake); (iii) for soil, a level of 81.1 pg/g TCDD equivalents (5% intake); and (iv) for food consisting of fish, poultry, pork and eggs, 29.6 pg/g (30% intake). No meat, milk and fruit analyses were provided in the Ontario analysis, consequently, the Connecticut food apportionment was adjusted to 50%, and air to 40%.

For the air medium (40% apportionment), the matrix was considered to include both vapor and particulate phases (the ambient air quality standard takes into account both phases). Dioxins and furans released from a variety of combustion sources have been shown to exist in vapor and particulate phases [15]. The vapor phase, as well as the particulate phase (assumed to be 100 percent in the respirable range) represent an inhalation hazard. Moreover, volatilization from the background and atmospheric transport of these semivolatile organics can potentially add to inhalation exposure. Based on sampling data and modeling, 2,3,7,8-TCDD in the urban air has been reported to exist in the particulate phase between 40 and 80 percent [16] whereas the octaisomer is 100 percent particle bound.

The vapor phase half-life through photolysis has been reported to be under six hours, and for the particulate phase the half-life is several hundred hours. At locations close to the spectrum of combustion sources exposure to vapor phase dioxins via inhalation can occur, in addition to direct inhalation of the respirable particulate phase. The background levels of dioxins in the vicinities of resource recovery facilities in Connecticut have been measured. The values (48 hr average) are: Mean = 0.045 pg/m^3 $\pm$ 0.77, Maximum = 0.719 pg/m^3, Range = 0.004 to 0.719 pg/m^3 dioxin equivalents, and N = 130. Fish samples (background monitoring) showed that the levels ranged from 0.23 to 8.95 pg/g for TCDF, and from a method detection limit of 0.05 to 6.15 pg/g for 2,3,7,8-TCDD. The monitored background data for Connecticut, although limited, indicate that both the atmospheric and food chain exposures are potentially significant human exposure pathways.

The settling velocity is an important factor in determining the significance of exposure pathways. Whereas the inhalation exposure pathway contributes to a constant absorbed dose (1 pg/m^3 x 20 m^3/day = 20 pg/day) from the vapor and particulate phases (this inhaled dose is independent of settling velocity), the dose estimate for the indirect food chain pathway is dependent on the settling velocity assumption. For example the Hart analysis [1] showed that the food chain contribution increased with increasing settling velocity from 56, 80, to 98 percent for settling velocities of 0.0003, 0.001, and 0.01 m/sec respectively, for the same ambient concentration.

The question arises as to the appropriate settling velocity to use in dose calculation. Travis et al's 1987 analysis used a settling velocity of 0.0023 m/sec and 100 percent particle-phase distribution to estimate the food pathway's contribution to total daily intake (98 percent). [3] On the other hand, a settling velocity of 0.001 m/sec was used in the Hart document to estimate the food chain contribution (80 percent). [1] Additionally, if the particle phase distribution were to be factored into the calculation (40 to 80 percent for 2,3,7,8-TCDD) then the food chain pathway percent contribution would be in the 56 to 72 percent range. Connecticut's 40 percent relative source contribution from air, and 50 percent from food to the daily

2025546094

dioxin intake are consistent with an average settling velocity of 0.001 m/sec, and 60/40 particle-vapor phase distribution assumptions. It should be emphasized that the exposure assessment and dose apportionment for the Connecticut assessment are based on the assumption that direct inhalation intake is from vapor and particulate phases, and the indirect intake is primarily from the particulate phase. The apportioned daily dosing rate associated with air exposure is 0.72 pg/kg/day (40 percent of 1.8 pg/kg/day). The equivalent dioxin concentration in ambient air is 2.2 pg/m^3 (0.72 pg/kg/day x 60 kg/20 m^3 per day). The calculations and conversions are based on the dose limit of 1.8 pg/kg/day.

DEP RISK MANAGEMENT

The DEP considered the DHS assessment, the Hart assessment and their factors in the risk management phase.

Connecticut DEP reviewed a range of health-based estimates for a dioxin equivalent AAQS - 0.1 to 2.2 pg/m^3. The lower bound value (0.1 pg/m^3) comes from the initial Hart analysis and the upper bound, from the DHS analysis. DEP decided to reduce by a factor of 2.2 the highest concentration in the range and derived a level of 1 pg/m^3. This dioxin equivalent concentration of 1 pg/m^3 was proposed and adopted as the AAQS.

The DEP management decision to apply an additional safety factor of 2.2 was based on the desire for an added margin of protection against potential carcinogenic and immunotoxic effects and on operating considerations. This safety factor assured that no exceedences of the health-based limit would occur through indirect and background exposures. According to DEP, the decision considered other management inputs, such as monitoring and enforcement as well as analytical and statistical considerations.

The following analysis explains the health rationale for the 2.2 factor and shows how the standard of 1 pg/m^3 is protective of human health: At the maximum ambient dioxin concentration of 1 pg/m^3 from <u>all</u> combustion sources, the daily inhaled dose can be estimated to be 0.33 pg/kg/day (60 kg human body weight and 20 m^3 air breathed in a day). This calculated dose represents about 18 percent of the health-based limit of 1.8 pg/kg/day. The Hart document provided an estimate of the indirect contribution from 1 pg/m^3 air dioxin concentration to be about 1.0 pg/kg/day (100 percent particle phase assumption and 0.001 m/sec settling velocity). This intake is 55 percent of the limit. Adjusting for 40 to 80 percent particle phase, the indirect dose can be estimated to be 0.4 to 0.8 pg/kg/day (22 to 44 percent of the limit). Additionally the background can potentially contribute to an estimated 0.45 pg/kg/day (25 percent of the limit). Thus, the direct (inhaled), indirect, and background intakes can contribute up to 65 to 98 percent of the health-based limit. If the 2.2 safety factor is not applied to the 2.2 pg/m^3 estimate, a potential doubling of the dose would occur and the target limit would be exceeded. A higher safety factor (10) was considered not necessary since DEP proposed to regulate individual sources through an emission standard that ensures each source will have an insignificant impact on ambient air. The dioxin AAQS 1 pg/m^3 is thus considered to be protective of public health.

DIOXIN EXPOSURE AND CANCER RISK

The potential cancer risks from chronic exposure to dioxins via ingestion (indirect pathway) and inhalation (direct pathway) were evaluated. The calculation used the standard approach that the product of the exposure dose (pg/kg/day) and the potency value represents the potential upperbound risk.

the diet were 0, 1.8 (50 ppt) and 18 ng/kg/day (500 ppt) up to 9 months. Following 7 months of treatment, the females were mated with untreated males. At the higher dose (18 ng/kg/day), there was a decrease in serum estradiol and progesterone. The menstrual cycle was however not affected. Only three animals conceived, after which two aborted and one had a normal birth. At the 1.8 ng/kg/day dose serum estradiol and progesterone levels were normal. Eight treated females were mated with untreated males; there were six pregnancies, four abortions and two normal births. DHS judged that the results of the sensitive rhesus monkey studies could potentially support a more conservative effect level than that reported in the rat studies. Accordingly, the 1.8 ng/kg/day lowest effects level was used to calculate a health-based limit on the total dioxin daily intake from multimedia exposure.

Besides reproductive effects, tumorogenic effects have been observed in rodent experiments following chronic exposure to low levels of 2,3,7,8-TCDD. For example, Kociba et al's 1978 two year study tested cancer response in rats at doses of 1, 10, and 100 ng/kg/day. The 10 ng/kg/day dose caused a statistically significant increase in liver tumors in experimental animals versus controls.[9]

A comparison of the rodent dose-response data from the cancer study by Kociba [9] and reproductive study by Murray [6] showed that the two experimental adverse outcomes observed in separate bioassays, reduced fertility and liver tumors, appear to be the result of exposure to equi-toxic doses of 2,3,7,8-TCDD, i.e., 10 ng/kg/day. The experimental exposure durations were different, 3 months for first reproductive effects, and 24 months for tumor effects (time to fatal tumor data are not available). For a congener like 2,3,7,8-TCDD, the cumulative dose is more critical than the dose rate.[10] The data from reproductive and cancer bioassays support this view. By factoring the exposure duration and calculating the cumulative dose for each outcome, it can be shown that 12 to 25 percent of the cumulative cancer dose causes fertility effects in the same species. The cumulative dose analysis suggests that the potential adverse reproductive effects from dioxin exposure present a substantial immediate concern and cancer is a chronic concern at the same levels of exposure. The data from the rhesus monkey studies by Allen et al [7] provide further support to the argument that the reproductive response is a very sensitive response. The experimental evidence points to a lower Lowest Observed Effect Level (LOEL), 1.8 ng/kg/day, compared with a LOEL of 10 ng/kg/day, identified in the rat studies. Factoring these values, and the exposure duration of six months in the non-human primate studies, and three months in the rat reproductive bioassays, even a smaller fraction, approximately 40 percent, of the cumulative administered dose (rats) can be estimated to elicit adverse reproductive effects in rhesus monkeys, i.e., the latter species exhibits 2-3 fold greater sensitivity than the rodent species. The cumulative dose response analysis places the sequence of health concerns - reproductive, developmental and carcinogenic in perspective.

A further concern arose from the experimental observations of Moore et al which showed that high levels of the unmetabolized dioxin congener, 2,3,7,8-TCDD, were excreted in milk and that each rat pup actually received a higher dose during the first week after birth than was administered initially to the mother.[11] This study revealed that while TCDD crosses the placenta in the rat, exposure of the offspring occurs mainly through nursing. Thus the maternal milk pathway is a significant pathway affecting neonatal development in rats. Dioxins have been detected in human breast milk but there is no evidence to link dioxin exposure through nursing to human neonatal developmental toxicity. It was concluded that the animal data on reproductive effects can be used to derive a total dose limit to human exposure in 2,3,7,8 - TCDD equivalents. Thus, the reported LOEL 1.8 ng/kg/day